The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ROY R. LOBB and LINDA C. BURKLY

Appeal No. 2005-0415
Application No. 09/251,073

MAILED
APR 28 2005
U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

ON BRIEF[1]

Before ELLIS, ADAMS, and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3, 6, 7, 9-13, 17, 18 and 26-37, which are all the claims pending in the application.[2]

Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A method for the treatment of allergic asthma comprising:
identifying a mammal suffering from allergic asthma; and

[1] Appellants waived their request for oral hearing. See Paper received March 7, 2005. Accordingly, we considered this appeal on Brief.

[2] Notwithstanding the examiner's statement (Answer, page 3), "[t]he copy of the appealed claims contained in the Appendix to the Brief is correct," the Appendix to the Brief does not reproduce claim 10 on appeal. For clarity, we note that claim 10 on appeal is drawn to "[t]he method of claim 1, wherein the mammal is human."

administering to the mammal a composition comprising a soluble fibronectin polypeptide.

The references relied upon by the examiner are:

Kogan et al. (Kogan)	5,510,332	Apr. 23, 1996
Wayner	5,730,978	Mar. 24, 1998
Arrhenius et al. (Arrhenius) (102(e) date Dec. 2, 1994[3])	6,117,840	Sep. 12, 2000

GROUND OF REJECTION

Claims 1-3, 6, 7, 9-13, 17, 18, and 26-37 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Wayner, Kogan and Arrhenius, as well appellants' acknowledged prior art at pages 1-3, 7 and 8 of the specification.

We affirm.

CLAIM GROUPING

According to appellants (Brief, page 2), "[c]laims 1-3, [6,[4]] 7, 9-13, 17, 18, and 26-37 stand or fall together." Since all claims stand or fall together, we limit our discussion to representative independent claim 1. Claims 2-3, 6, 7, 9-13, 17, 18 and 26-37 will stand or fall together with claim 1. 37 CFR §1.192(c)(7), now 37 § CFR 41.67(c)(7).

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[3] We note that Arrhenius was filed on Apr. 14, 1997 as a continuation of Application No. 08/349,024, filed December 2, 1994, now abandoned, which was a continuation-in-part of Application No. 08/164,101, filed December 6, 1993, now abandoned. There is no evidence on this record that the examiner considered whether Arrhenius is entitled to the December 6, 1993 priority date. Accordingly, we have considered the merits of Arrhenius based on the December 2, 1994 effective filing date.

[4] Appellants do not list claim 6 in their "Grouping of Claims." Appellants, however, do not provide a separate argument for claim 6. Accordingly, notwithstanding the examiner's statement (Answer, page 2), "[t]he examiner is in agreement with appellant's [sic] statement that claims 1-3, 7, 9-13, 17, 18 and 26-37 stand or fall together," we find that claim 6 stands or falls together with claims 1-3, 7, 9-13, 17, 18 and 26-37. 37 CFR §1.192(c)(7), now 37 § CFR 41.67(c)(7).

BACKGROUND

Claim 1 is drawn to a method for the treatment of allergic asthma. The method comprises two steps: (1) identifying a mammal suffering from allergic asthma, and (2) administering to the mammal a composition comprising a soluble fibronectin polypeptide.

According to appellants' specification (page 2, emphasis added),

> [i]n allergen-induced asthma, sufferers often exhibit a dual response to exposure to an allergen -- an "early phase" response beginning immediately after exposure and lasting until 1-2 hours after exposure, followed by a "late phase" response beginning about 3 hours after exposure and lasting sometimes until 8-10 hours or longer after exposure. (D.W. Cockroft, 1990 [4].)[.] Late phase response in allergen-induced asthma and persistent hyperresponsiveness have been associated with the recruitment of leukocytes, and particularly eosinophils, to inflamed lung tissue. (W.M. Abrahann et al., 1988 [8].)[.]

Inflammatory leukocytes are recruited to sites of inflammation in the late phase response by

> cell adhesion molecules that are expressed on the surface of endothelial cells and which act as receptors for leukocyte surface proteins or protein complexes. Eosinophils have recently been found to participate in three distinct cell adhesion pathways to vascular endothelium, binding to cells expressing intercellular adhesion molecule-l (ICAM-1), endothelial cell adhesion molecule-l (ELAM-l), and vascular cell adhesion molecule-l ([V]CAM-1). (P.F. Weller et al., 1991 (10); G.M. Walsh et al., 1991 [11]; B.S. Bochner et al., 1991[12]; and A. Dobrina et al., 1991 [13].)[.] VCAMl binds to the $\alpha_4\beta_1$, integrin, VLA-4, which is expressed on various lymphoid cells, including eosinophils (Weller et al., 1991 [10]; Elices et al. 1990 [14]). That eosinophils express VLA-4 differentiates them from other inflammatory cells such as neutrophils, which bind to ELAM-l and ICAM-l but not VCAM-l.

Specification, page 3, emphasis added.

Accordingly, appellants' invention provides for the treatment of allergic asthma by "administering to an asthma sufferer an effective amount of a VLA-4 blocking agent." Id. According to appellants' specification (page 9), "a VLA-4 blocking agent is a molecule [that] ... coats, or binds to, a VLA-4-ligand, e.g., VCAM-1 or fibronectin, with sufficient specificity to inhibit the VLA-4/VLA-4-ligand interaction...." With regard to fibronectin, appellants' disclose (specification, page 9, as amended May 13, 2002), "these binding agents include soluble ... fibronectin, fibronectin having an alternatively spliced non-type III connecting segment, and fibronectin peptides containing the amino acid sequence EILDV (SEQ ID NO:16)...."

DISCUSSION

The examiner finds (Answer, page 3), claim 1 unpatentable over Wayner, Kogan and Arrhenius, taken together or separately, in view of the admitted prior art as set forth at pages 1-3, 7 and 8 of appellants' disclosure.

Wayner:

According to the examiner (Answer, page 4), Wayner "teach[es] methods of suppressing the immune response in human patients, including chronic and relapsing inflammation, including asthma[, as well as allergy,] by interfering [with] the binding of receptor-ligand interactions between lymphocytes and endothelial cells...." The examiner finds (id.), Wayner "teach[es] that the inhibitory peptide comprising fibronectin, a portion of fibronectin including the fibronectin alternatively spliced IIICS region including the CS-1 domain comprising the

EILDV motif ... blocks adhesive events, including those with [$\alpha_4\beta_1$] expressing lymphocytes and endothelial cells...."

Kogan:

According to the examiner (id.), Kogan "teach[es] methods of treating diseases associated with uncontrolled migration of white blood cells to damaged tissues such as asthma[, as well as allergy[5],] by inhibiting the binding of [$\alpha_4\beta_1$] to VCAM-1...." In addition, the examiner finds (Answer, page 5), Kogan teach[es] $\alpha_4\beta_1$ "recognizes fibronectin, including fibronectin isoforms including the CS1 peptide present in the alternatively spliced Type III connecting segments...."

Arrhenius:

According to the examiner (id.), Arrhenius "teach[es] methods of blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. [$\alpha_4\beta_1$]) to inhibit inflammatory responses, including asthma, [and] asthmatic lung...." In addition, the examiner finds (id.), Arrhenius "teach[es] the use of fibronectin and fibronectin derived peptides such as CS-1 and SEQ ID NO: 3 to block various inflammatory conditions by blocking the interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. [$\alpha_4\beta_1$])...." In this regard, the examiner finds that Arrhenius exemplify the treatment of asthmatic rabbits which according to the examiner "rely upon early phase and late phase allergic reactions (see [Arrhenius,] Example 5 on columns 33-34). Answer, page 6.

Based on this evidence the examiner finds (id.), Wayner, Kogan and Arrhenius "all recognized" the use of fibronectin inhibitors to treat "both asthma

and allergy at the time the invention was made...." According to the examiner (id.),

> [t]he well known practices of the ordinary artisan in the treatment of asthma, including allergen-induced asthma at the time ... [of appellants'] invention, was consistent with the treatment of asthma ... [with] fibronectin-derived inhibitors which block the interactions between [$\alpha_4\beta_1$] and its receptor between lymphocytes and endothelial cells in order to inhibit inflammatory responses as taught by Wayner et al., Kogan et al. and/or Arrhenius et al.

Therefore, the examiner concludes (id.), "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to select fibronectin-derived peptides, including those comprising EIDLV to treat asthma, including allergen-induced asthma by inhibiting the interaction between lymphocytes and endothelial cells." According to the examiner (Answer, page 7), "[f]rom the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention." Thus, the examiner concludes (id.), in the absence of evidence to the contrary, "the invention as a whole was prima facie [sic] obvious to one of ordinary skill in the art at the time the [appellants'] invention was made...."

In response, appellants assert (Brief, page 3), "nothing in the prior art of record would have led the artisan to pick and choose the specific aspects from the references and modify them to administer a soluble fibronectin polypeptide to a patient suffering from allergic asthma with a reasonable expectation of success." While appellants recognize that "[b]oth Wayer and Kogan broadly disclose diseases that might be treated by inhibiting [$\alpha_4\beta_1$] integrin binding,"

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[5] See Answer, page 5.

appellants argue that "nothing in Wayner and/or Kogan provides motivation to one of skill in the art to specifically administer a soluble fibronectin polypeptide for the treatment of allergic asthma." Brief, page 3. In this regard, appellants assert (Brief, bridging sentence, pages 3-4), "one of skill in the art would not reasonably expect that a single compound, e.g., a soluble fibronectin polypeptide, would be successful in the treatment of all of the diseases, or even most of the diseases, disclosed in Wayner and Kogan." Appellants also argue (Brief, page 4), "Arrhenius does not use soluble fibronectin polypeptides as required by the claims, but instead uses highly modified peptidomimetic agents...." In this regard, appellants assert (id.), "Arrhenius teaches away from fibronectin polypeptides, such as CS-I peptides, by describing their drawbacks and stating ... that the CS-I peptide 'is large and costly to make, and also is subject to rapid degradation.'"

For the following reasons we are not persuaded by appellants' arguments. As appellants disclose at page 2 of their specification, it was known in the art prior to the date of appellants' invention that the "[l]ate phase response in allergen-induced asthma ... [is] associated with the recruitment of leukocytes, and particularly eosinophils, to inflamed lung tissue." Further appellants disclose at page 3 of their specification, it was known in the art prior to the date of appellants' invention that "[i]nflammatory leukocytes are recruited to sites of inflammation by cell adhesion molecules that are expressed on the surface of endothelial cells and which act as receptors for leukocyte surface proteins or protein complexes." With regard to eosinophils, appellants disclose id., it was

known in the art prior to the date of appellants' invention that "[e]osinophils participate in three distinct cell adhesion pathways to vascular endothelium, binding to cells expressing ... ICAM-1 ... ELAM-1 ... [and] [V]CAM-1. ... VCAM[-]1 binds to the $\alpha_4\beta_1$, integrin, VLA-4, which is expressed on various lymphoid cells, including eosinophils...."

Wayner:

> Wayner disclose (column 7, lines 8-29, emphasis added):
>
> The invention is based upon the discovery that the $\alpha_4\beta_1$ extracellular matrix receptor promotes adhesion of lymphocytes to endothelial cells via attachment to a defined peptide sequence. ... By preventing the interaction between the $\alpha_4\beta_1$ receptor and its ligands using ... defined peptide sequences, the present invention enables, for the first time, specific intervention in the migration of lymphocytes through the vascular endothelium and into tissues. The present invention, therefore, has particular clinical utility in suppression of the immune response; ... the adherence of lymphocytes to endothelium may be inhibited systemically, or may, alternatively, be localized to particular tissues or circumscribed areas. Accordingly, the present invention provides for treatment of diseases ... of the immune system, including asthma....

According to Wayner (column 7, lines 30-32), "[t]he $\alpha_4\beta_1$ integrin is a lymphocyte receptor for the carboxy terminal cell binding domain ... of fibronectin...."

Further Wayner disclose (column 15, lines 23-27, emphasis added), "[a]s exemplified in Section 7, infra, ... the peptide EILDVPST ... was able to competitively inhibit the binding of lymphocytes to fibronectin and to endothelial cells." In this regard, we note that according to appellants' specification (page 9, as amended May 13, 2002, emphasis added), blocking agents used in methods of the invention [include] soluble forms of ... fibronectin, fibronectin having an

alternatively spliced non-type III connecting segment, and fibronectin peptides containing the amino acid sequence EILDV...." Similarly, Wayner disclose (column 17, lines 21-35),

> [t]he peptides of the invention include any peptide which is capable of interacting with the E[xtra]C[ellular]M[atrix]R[eceptor] of interest. In a specific embodiment of the invention, any peptide which is capable of interacting with the $\alpha_4\beta_1$ receptor may be used to inhibit the binding of lymphocytes to endothelium. ... In a most preferred embodiment, the peptides of the invention comprise at least a portion of the sequence EILDVPST....

Thus Wayner disclose (column 16, lines 15-26),

> [t]he method of the invention is therefore useful in preventing the egress of lymphocytes through the vascular endothelium and into tissue. Accordingly, the present invention provides for a method of suppressing the immune response in human patients in need of such treatment. In particular embodiments, the present invention provides for methods of treatment of diseases associated with chronic or relapsing activation of the immune system, including ... asthma, and allergy....

Thus, as we understand it, Wayner discloses a method of using a soluble fibronectin polypeptide to prevent the egress of lymphocytes through the vascular endothelium and into tissue, thereby providing for a method of treating asthma. Wayner disclose that the mechanism through which the egress of lymphocytes through the vascular endothelium and into tissue is prevented is by the use of a peptide, e.g., a soluble fibronectin polypeptide, which is capable of interacting with the $\alpha_4\beta_1$ receptor. As discussed above, appellants admit that it was known in the art prior to the date of their invention that eosinophils migrate through a pathway that involves VCAM-1 binding to $\alpha_4\beta_1$. In addition, appellants admit that it was known in the art prior to the date of their invention that the late

phase response in allergen-induced asthma is associated with the recruitment of leukocytes and particularly eosinophils, to inflamed lung tissue.

Therefore, in our opinion, the evidence of record weighs in favor of affirming the examiner. Accordingly, we find that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to treat allergic asthma by administering to a mammal a composition comprising a soluble fibronectin polypeptide, specifically a polypeptide that comprises at least a portion of the sequence EILDVPST[6], taught by Wayner.

We are not persuaded by appellants' assertion that Wayner's in vitro data would not provide a person of ordinary skill in the art with a reasonable expectation of success in treating allergic asthma with a soluble fibronectin polypeptide. In this regard, we note that obviousness does not require absolute predictability of success. For obviousness, all that is required is a reasonable expectation of success. In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Absent evidence to the contrary, which we find none, it is our opinion that Wayner, in combination with appellants' admitted prior art, provides a reasonable expectation of successfully treating allergic asthma with a soluble fibronectin polypeptide. We remind appellants that

[6] Note appellants' claim 26 on appeal, is drawn to "[t]he method according to [c]laim 1, wherein the soluble fibronectin polypeptide comprises an EILDV motif (SEQ ID NO.:16)." Thus, it appears that the scope of the term "soluble fibronectin polypeptide" as it appears in claim 1 on appeal, includes a polypeptide that comprises at least a portion of the sequence EILDVPST as taught by Wayner.

attorney argument cannot take the place of evidence lacking in the record. Meitzner v. Mindick, 549 F.2d 775, 782, 193 USPQ 17, 22 (CCPA 1977).

Accordingly, we affirm the rejection of claim 1 under 35 U.S.C. § 103 as unpatentable over Wayner in view of appellants' acknowledged prior art. As discussed supra claims 2-3, 6, 7, 9-13, 17, 18 and 26-37 fall together with claim 1.

For the reasons enumerated by the examiner, we find Kogan and Arrhenius to be cumulative to the teaching of Wayner. Accordingly, we do not reach the merits of the rejection as it applies to Kogan and Arrhenius.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Joan Ellis
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

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